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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/589,288	06/08/2000	Guo-Liang Yu	PF343P3C5	1519

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EXAMINER
PRASAD, SARADA C

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 08/13/2002 13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/589,288	YU ET AL.	
	Examiner	Art Unit	
	Sarada C Prasad	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 May 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *85-91,118-124 and 148-182* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *85-91,118-124 and 148-182* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

1. Receipt of Applicants' arguments and amendments filed in Paper No. 11 (5/3/02) is acknowledged. Supplemental IDS (Paper No. 12), replacement of sequence listing are also acknowledged. As per applicants' request, claims 1, 17, 19, 26-84, 92-117 and 125-147 have been cancelled, amendments to claims 85, 118, 148, 158 have been entered, new claims 165-182 have been added, and currently claims 85-91, 118-124, 148-182 are pending and are under consideration for examination.

2. Applicant's arguments filed in Paper No. 11 (5/3/02), have been fully considered but were deemed persuasive in part. The issues remaining are stated below. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

3a. New title is acknowledged.

3b. Substitute specification (Paper No. 11) has been entered.

Claim Rejections - 35 USC § 112 first paragraph

Scope of Enablement

4b. Claims 85-91, 118-124, 148-182 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting B-lymphocyte proliferation comprising administering to an individual, a therapeutically effective amount of an antagonistic antibody or a portion thereof that specifically binds a protein consisting of an amino acid sequence of amino acids residues 134-285 of SEQ ID No. 2, does not reasonably provide enablement for a method of inhibiting differentiation, and survival of B lymphocytes or

proliferation, differentiation, and survival of 'all other' leukocytes, or treatment of 'any autoimmune diseases' as set forth in Paper No. 8 (11/6/01) and reiterated as follows.

Response to Applicants' arguments:

Applicants' arguments addressing lack of support from specification regarding the selection of patient population, or what are the symptoms that should be alleviated (paragraphs bridging pages 10-11 of Paper No. 11, 5/3/02,), and regarding the specificities of neutrokine-α antibodies used for administration (page 11, antibodies of the invention are fully enbaled) are found to be persuasive.

Instant claims 85-91, 165, 118-124, 166-173, 174-180 are drawn to methods of treating diverse autoimmune diseases or disorders comprising administering to an individual a therapeutically effective amount of an antagonistic antibody or portion thereof that specifically binds a protein consisting of an amino acid sequence of SEQ ID No. 2, or amino acid residues 134-285 of SEQ ID No. 2. The claim language encompasses treatment of 'any and all' autoimmune diseases, while the disclosure only sets forth for stimulation of B cells and antibodies to neutrokine-α. Applicants extrapolate these two aspects and assert that antibodies to neutrokine-α inhibit its ability to stimulate B cell proliferation and this assertion has been found to be persuasive. However, the specifcation is not enabling for a method of treatment of all autoimmune diseases.

Applicants' arguments regarding lack of enablement of instant specifcation for a method of treatment of all autoimmune diseases or any particular autoimmune diseases (page 10, entire 2nd para, Paper No. 11) recited as follows

'neutrokine-α levels in serum and/or synovial fluid correlate with models of autoimmunity as well as human autoimmune syndromes, including immune based rheumatic diseases including rheumatoid arthritis, systemic lupus erythematosus, and Sjogern's syndrome. The observation that elevated levels of neutrokine-α are associated with several human and mouse autoimmune syndromes has led those skilled in the art to state that neutrokine-α blocking agents hold great promise in the treatment of autoimmunity. Such treatment was found to alleviate symptoms in mice. Together, these facts demonstrate that it is feasible for one of skill in the art to treat autoimmune diseases with neutrokine-α blocking agents such as antagonistic antibodies'

have been given full consideration.

These arguments are not found to be persuasive because the guidance provided is not adequate for one of skill to practice the invention as that of the filing date of instant application. Specification discloses the ability of neutrokine-α to stimulate B lymphocytes (Example 7), and contemplates that neutrokine-α levels could be expressed at lower or higher levels in various diseases (page 23, lines 17-20 of specification), and makes assertions regarding administration of neutrokine-α or its antibodies as needed in each of the instances respectively. Applicants rely on the post filing date art (references cited 1-7 in Paper No. 11) immensely and make assertions on use of antibodies to neutrokine-α for treatment of all autoimmune diseases where high levels of immunoglobulins might be observed (page 330 of specifcation). However, the specification did not teach or contemplate that in any one or all of the autoimmune diseases elevated levels of neutrokine-α would be expected. Specification discloses neutrokine-α levels in immune cells (Table V, in pages 422-423) and has not provided any clues about what types of levels to expect in auto imune patients. Also, the specification has not provided any information or guidance regarding extrapolation from inhibition of B cell proliferation in vitro mediated by neutrokine-α by mere administration of the instant antagonistic antibodies directed to various regions of

neurokine-α, so one of skill could extend their use for the treatment of autoimmune diseases. State of the art acknowledges that autoimmune diseases are characterized by higher levels of IgG levels. However, in the absence of knowledge of higher levels of neutrokine-α and the role it plays, if any, in either rheumatoid arthritis, or SLE, or any other autoimmune disease, at the time the invention was made, one of skill would not reasonably expect the instant antagonistic antibodies to neutrokine-α to have an ameliorative effect in autoimmune diseases. Furthermore, the specification also has failed to disclose evidence that blocking of neutrokine-α with antibodies would predictably lead to alleviating symptoms of autoimmune diseases. In the instant case, enablement of all the claims rests on two facts that neutrokine-α can stimulate B cell proliferation (at the time of filing), and BAFF is expressed in higer levels in autoimmune diseases (post filing date art). These two facts are not sufficient for one of skill to successfully achieve inhibition of B cell proliferation by the antibody to neutrokine-α, and effectively to treat all autoimmune diseases, because increased B cell activity is not the only criterion of all autoimmune diseases, and neutrokine-α is not the only stimulant of B cells, particularly B cells directed to produce antibodies to self antigens as in autoimmune diseases.

Claims 148-164, 181-182 are directed to a method of inhibiting leukocyte proliferation, differentiation, or survival comprising administering to an individual a therapeutically effective amount of an antagonistic antibody or portion thereof that specifically binds a protein consisting of an amino acid sequence selected form the entire sequence of SEQ ID NO. 2. The specification is not enabling for the practice of these claims, because it is only the B lymphocyte proliferation that the instant neutrokine-α predictably stimulates and not proliferation of all leukocytes. In fact, the term 'Leukocytes' represents three lines of development from primitive

elements: myeloid, lymphoid, and monocytic series which include monocytes, B and T lymphocytes, neutrophils, eosinophils, and basophils (Stedman's medical dictionary). Therefore, recitation of leukocytes in the instant claims is extremely broad, and the specifcation is not enabled for one of skill to obtain inhibition of stimulation of all of these cells by the instant antibodies to neutrokine-α.

It is believed that all of applicants' arguments have been addressed. Based on the above discussion, rejection of claims under 35 USC 112 first paragraph is maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarada C Prasad whose telephone number is 703-305-1009. The examiner can normally be reached Monday – Friday from 8.00 AM to 4.30 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sarada Prasad, Ph.D.
Examiner
Art Unit 1646
August 9th, 2002.

Yvonne Eyler
YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
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